## REMARKS

In the response to the Office Action of August 6, 2008, Applicants have amended claim 21 to recite that the claimed attenuated live parasite comprises a ribosomal protein gene under the control of an inducible promoter, by which the promoter can be switched on and off regulating the expression of the ribosomal protein gene to limit ribosome synthesis, which limits parasite replication in infected cells. Support for this amendment is found in the specification on page 5, lines 21-33.

Claims 21, 28-32 and 34-35 stand rejected under 35 U.S.C. § 102(b) for anticipation by Wirtz et al. It has been asserted that Wirtz et al teach the inducible expression of transgenes including ribosomal protein genes in *Trypanosome* mediated by the Tet repressor (tetR) inserted in the inducible PARP promoter.

The rejection over Wirtz et al is respectfully traversed. Applicants respectfully submit that Wirtz et al did not teach the regulation of ribosomal protein genes but, instead, the regulation of heterologous genes. Although the heterologous gene may be inserted in the vicinity of the ribosomal RNA genes they are not themselves regulated. More importantly, perhaps, the ribosomal genes code for ribosomal RNA, they are not translated to encode any ribosomal proteins. In the *Leishmania* gene genome of Wirtz et al, the ribosomal protein genes are located in a different section of the genome from that wherein the heterologous genes are inserted. Consequently, there is no regulation of a ribosomal protein gene suggested by Wirtz et al.

Claims 21-27 and 29-31 stand rejected under 35 U.S.C. § 103(a) for obviousness over Sutherland et al in view of Xu et al. Sutherland et al are said to teach the attenuation of *Theileira* cell lines and other avirulent Apicomplexan protozoa and the desire and need to control gene expression in such parasites. It is said, however, that Sutherland et al did not teach that the parasites comprised a ribosomal protein gene under the control of an inducible promoter. Xu et al is said to teach the expression of genes whose products have a harmful effect and the desire and need to control gene expression in a wide variety of expression systems. It was concluded, therefore, that it would have been prima facie obvious in view of the attenuated live parasite of

Sutherland et al to incorporate a ribosomal protein gene under the control of the inducible promoter taught by Xu et al.

The rejection over Sutherland et al taken with Xu et al is respectfully traversed. Applicants respectfully submit that there is no suggestion of controlling ribosomal protein expression in a parasite with a gene under the control of an inducible promoter. There is no suggestion that an attenuated live parasite can be limited in its replication in infected cells by controlling ribosome synthesis through the regulation of the expression of ribosomal protein genes.

Claims 21, 28-32 and 34-35 stand rejected under 35 U.S.C. § 103(a) for being obvious over Titus et al in view of Yan et al. Titus et al is relied on for teaching the development of a safe, live, attenuated *Leishmania* vaccine by gene replacement, although Titus et al do not teach *Leishmania* comprising a ribosomal protein gene under the control of an inducible promoter. Yan et al is relied for teaching tetracycline regulated gene expression in *Leishmania* with an inducible system that provides stringent regulation of gene expression in *Leishmania* while offering great advantages.

The rejection of claims 21, 28-32 and 34-35 over Titus et al in view of Yan et al is respectfully traversed. The present claims, as now amended, are directed to attenuated, live parasites wherein a ribosomal protein gene is under the control of an inducible promoter, the promoter being able to be switched on or off, which regulates the expression of ribosomal protein genes, whereby ribosome synthesis is limited, thereby limiting parasite replication in infected cells. The result of limiting ribosome synthesis, and therefore the replication of the parasite itself after infecting cells, is not suggested in the prior art. Accordingly, there would be no suggestion of using procedures that may be found in the prior art to use an inducible promoter to control the expression of the ribosomal protein gene. Accordingly, the ordinary practitioner would find no suggestion in the prior art to prepare the modified parasite as presently claimed.

Claim 33 stands rejected under 35 U.S.C. § 112, second paragraph, for being indefinite. The Examiner objected to the use of the term "preferably" in the claim.

With the present amendment to claim 33 it is believed that this rejection is overcome.

In view of the above, with the present amendments to claims 21 and 33, it is believed that

claims 21-35, all claims in the application, are in condition for allowance.

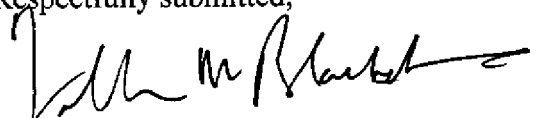
Applicants wish to thank the Examiner for her helpful suggestions resulting in the present amendments.

Pursuant to 37 C.F.R. § 1.116, Applicants submit that the amendments presented herein are made to i) cancel claims or comply with any requirement of form expressly set forth in a previous Office action, or ii) present rejected claims in better form for consideration on appeal.

Should the Examiner believe that a conference would be helpful in advancing the prosecution of this application, she is invited to telephone Applicants' attorney at the number below.

Applicants do not believe that any other fee is due in connection with this filing. If, however, Applicants do owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No. **02-2334**. In addition, if there is ever any other fee deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. **02-2334**.

Respectfully submitted,



William M. Blackstone, PTO Reg. No. 29772
Chief Patent Counsel
Intellectual Property - Animal Health
Global Law and Public Affairs
Schering-Plough

Intervet Inc.
P.O. Box 318
29160 Intervet Lane
Millsboro, Delaware 19966-0318
United States

(302) 934-4317 (tel)
(302) 934-4305 (fax)

WMB:dap